CLAIMS

1. A stable intermediate suitable for covalent conjugation with a biologically active material, said intermediate having the formula $P\text{-}O\text{-}CH_2\text{-}CH_2\text{-}SO_2\text{-}(CH=CH_2)_n$, wherein n is an integer and is at least 1, and P represents a hydrophilic biopolymer having a functional group capable of reacting with divinyl sulfone.

2. An intermediate as claimed in claim 2 wherein the biopolymer is a hyaluronan moiety, or a moiety of a mixture of a hyaluronan with at least one other hydrophilic polymer.

3. An intermediate as claimed in claim 2 wherein the hyaluronan has a molecular weight of about 1×10^3 to 1×10^7 Da.

4. An intermediate as claimed in claim 3 wherein the molecular weight is about 1×10^5 Da.

5. An intermediate as claimed in claim 3 wherein the hyaluronan is a hylan.

6. An intermediate as claimed in claim 5 wherein the hydrophilic biopolymer is a natural or synthetic polysaccharide selected from the group consisting of hydroxyethyl cellulose, carboxymethyl cellulose, xanthan gum, chondroitin sulfate and heparin, a protein selected from

the group consisting of collagen, elastin, albumin, a globulin, keratin sulfate, a sulfated aminoglycosaminoglycan and a synthetic water soluble polymer.

7. A conjugate comprising the reaction product of the intermediate having the formula P-O-CH_2- CH_2-SO_2-$(CH=CH_2)_n$, wherein n is an integer and is at least 1, and P represents a hydrophilic biopolymer and a biologically active material capable of being covalently and nucleophilically bonded to said intermediate.

8 A conjugate according to claim 7 wherein the biologically active substance is any such substance having at least one chemical group reactive toward DVS.

9. A conjugate according to claim 8 wherein the hydrophilic biopolymer is a hyaluronan moiety or a moiety of a mixture of a hyaluronan with at least one other hydrophilic polymer.

10. A conjugate according to claim 8 wherein the biologically active material is an antineoplastic, an antibiotic, a protein, an enzyme or a peptide.

11. A conjugate according to claim 10 wherein the antineoplastic is vinblastin or paclitaxel, the antibiotic is gentamicin, the protein is alpha- interferon or cytochrome C, the enzyme is thrombin and the peptide is avidin.

12. A conjugate according to claim 9 wherein the biologically active material is alpha-interferon.

13. A conjugate according to claim 12 and having the formula HA-O-CH_2- CH_2-SO_2-CH_2- CH_2-NH-INF, wherein HA represents a hyaluronan moiety or a moiety of a mixture of a hyaluronan with at least one other hydrophilic polymer, and INF represents an alpha-interferon moiety.

14 A method of preparing the intermediate having the formula P-O-CH_2- CH_2-SO_2-$(CH=CH_2)_n$, wherein n is an integer and is at least 1, and P represents a hydrophilic biopolymer having a functional group capable of reacting with divinyl sulfone comprising subjecting the hydrophilic biopolymer having a concentration of 0.01 to 1.0% at a temperature of about 4° C to treatment with divinyl sulfone in the presence of a carbonate buffer at a pH of about 9.6, for about 30 minutes, thereafter reducing the pH to about 6.5 with HCl to stop the reaction and leave free, unreacted vinyl groups covalently attached to the hydrophilic biopolymer through -OH groups thereon.

15. Amethod according to claim 14 wherein the hydrophilic biopolymer is a hyaluronan moiety or a moiety of a mixture of a hyaluronan with at least one other hydrophilic polymer.

16 A method according to claim 14 wherein the concentration is 0.2 to 1%.

17 A method according to claim 14 wherein the concentration of hydrophilic biopolymer in the aqueous solution is about 0.5%.

18 A method according to claim 17 wherein the hydrophilic biopolymer is a hyaluronan moiety or a moiety of a mixture of a hyaluronan with at least one other hydrophilic polymer.

19 A method according to claim 14 comprising removing the unreacted divinyl sulfone and

hydrolysis products of the reaction by dialysis.

20 A method of preparing the conjugate of claim 7 comprising reacting the intermediate with the biologically active material in aqueous solution at a pH of 9or higher at a temperature of about 4° C in the presence of a carbonate buffer and shaken for about 24 hours and thereafter dialyzing the reaction mixture with saline solution to remove therefrom unreacted biologically active material.

21 A method according to claim 20 wherein the biologically active substance is any such substance having at least one chemical group reactive toward DVS.

22. A method according to claim 20 wherein the intermediate has the formula P-O-CH_2- CH_2-SO_2-(CH=CH_2)$_n$, wherein n is an integer and is at least 1, and P represents a hydrophilic biopolymer and the hydrophilic biopolymer is a hyaluronan moiety or a moiety of a mixture of a hyaluronan with at least one other hydrophilic polymer.

23. A method according to claim 20 wherein the biologically active material is an antineoplastic, an antibiotic, a protein, an enzyme or a peptide.

24. A method according to claim 23 wherein the antineoplastic is vinblastin or paclitaxel, the antibiotic is gentamicin, the protein is alpha-interferon or Cytochrome C, the enzyme is thrombin and the peptide is avidin.

25. A method according to claim 20 wherein the biologically active material is alpha-interferon.

26. A pharmaceutical composition comprising a therapeutically effective amount of the conjugate according to claim 7 in a pharmacologically acceptable carrier or vehicle therefor.

27. A method of treating an animal afflicted with a neoplastic condition comprising administering a therapeutically effective amount of the pharmaceutical composition according to claim 26 to said animal.

28. A stable intermediate suitable for covalent conjugation with a biologically active material, said intermediate having the formula:

RO-CH2-CH2-SO2-CH2-CH2-O—(--CH2-CH2-SO2-CH2-CH2-O--)n—CH2-CH2-SO2-CH=,

wherein R is a carbohydrate, n is 0, 1, 2, 3, . . . and having a functional group capable of reacting with divinyl sulfone.

29. A conjugate comprising the reaction product of the intermediate as claimed in claim 28 and a biologically active material capable of being covalently and nucleophilically bonded to said intermediate.

30. A conjugate as claimed in claim 29 wherein the biologically active material is R'OH, wher ein R' is a drug mol ecule, water, a protein or an additional carbohydrate, and the conjugate has the formula:

RO-CH2-CH2-SO2-CH2-CH2-O—(--CH2-CH2-SO2-CH2-CH2-O--)n—CH2-CH2-SO2-CH2-CH2-OR.

31. A pharmaceutical composition comprising a therapeutically effective amount of the conjugate according to claim 30 in a pharmacologically acceptable carrier or vehicle therefor.